

### Remarks

In response to the Restriction Requirement mailed July 26, 2004, Applicant elects, with traverse, the claims in Group VIII (claims 28 and 32-39), directed to a method which detects or determines whether a nucleic acid sample has a specified mutation in a human TLR4 gene. Reconsideration of the Restriction Requirement, in view of the remarks presented below, is respectfully requested.

The Restriction Requirement is traversed on the basis that the inventions are so closely related. For instance, claims directed to a method which detects or determines whether a nucleic acid sample has a specified mutation in a TLR4 gene (claims 28 and 32-39; Group VIII) are clearly related at least to claims directed to a method of identifying a human at risk of, or having, an indication associated with altered innate immunity which detects or determines whether a nucleic acid sample has a specified mutation in a TLR4 gene (claims 16-19 and 32-39; Group II), and to claims directed to an isolated and purified DNA molecule comprising a human genomic DNA encoding TLR4, a biologically active fragment or a variant thereof; an isolated and purified nucleic acid molecule comprising a human nucleic acid segment encoding a variant TLR4, or a biologically active fragment thereof; an expression cassette comprising a promoter operably linked to a human DNA segment encoding a variant TLR4, or a biologically active fragment thereof; a host cell augmented by a nucleic acid molecule of the invention; and methods to prepare a variant TLR4 polypeptide (claims 1-15; Group I); claims directed to an isolated, variant human TLR4 polypeptide or a biologically active fragment thereof (claims 20-22; Group III); and a claim directed to a transgenic mouse encoding human TLR4 which is expressed so as to result in the transgenic mouse having altered innate immunity relative to a corresponding nontransgenic mouse having altered innate immunity relative to a corresponding nontransgenic mouse (claims 29-30; Group VII).

In particular, claims directed to a method which detects or determines whether a nucleic acid sample has a mutation at residue 299 or 399 in a TLR4 gene (claims 28 and 32-39; Group VIII) are clearly related to claims directed to a method of identifying a human at risk of, or having, an indication associated with altered innate immunity which detects or determines whether a nucleic acid sample has a mutation at residue 299 or 399 in a TLR4 gene (claims 16-

19 and 32-39; Group II).

The Restriction Requirement is also traversed on the basis that restriction requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. In light of this, it is submitted that Applicant should not be required to incur the additional costs associated with the filing of divisional applications in order to obtain protection for the claimed subject matter. In particular, evidence that the search and examination of the claims in at least Group VIII and Group II can be efficiently and effectively searched in a single search is provided in the Restriction Requirement, as the claims in Group VIII and Group II fall within the same class (class 435) for search purposes. Yet further evidence is found in the parent application to the present application, i.e., U.S. application Serial No. 09/329,515, now U.S. Patent No. 6,740,487, where claims corresponding to the claims in Groups VIII and II of the present application were grouped in one group and examined in the same application.

Thus, it is respectfully submitted that claims of at least Groups VIII and II can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

**RESPONSE TO RESTRICTION REQUIREMENT**

Serial Number: 10/010,066

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The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if there are any questions regarding this response or if prosecution of this application may be assisted thereby.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date September 22, 2004 By Janet E Embretson  
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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 23 day of September, 2004.

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